REMARKS/ARGUMENTS

Reconsideration and withdrawal of the rejections of the present application are respectfully requested in view of the amendments to the claims and remarks presented herewith, which place the application into condition for allowance.

Status of the Claims and Formal Matters

Claims 30, 32-35, 37-45, 47 and 49-71 are pending. Claims 46, 48 and 69 are cancelled. Solely for the purpose of expediting patent prosecution, claims 30, 32, 34, 35, 37, 38, 47, 49, and 51-56 are amended to clarify instant doses of SAHA and instant dosing schedules. These amendments are supported by the application as originally filed, and do not constitute new matter.

Rejections under 35 USC §103(a)

Claims 30, 32-35, 37-47 and 49-71 are as being rejected under 35 USC § 103(a) as being allegedly obvious over Richon et al (US 2003/0235588; "Richon") in view of Rubartelli et al (Cancer Research, 1995, vol.55, pages 675-680, "Rubartelli"). The Office Action contends that instantly claimed methods of treating B-cell lymphoma would have been allegedly obvious to one of ordinary skill in the art at the time the invention was made because Richon allegedly discloses oral formulations and doses of the instantly claimed HDAC inhibitor and Rubartelli allegedly provides the nexus and motivation to use the methods disclosed in Richon to treat lymphomas. Applicants traverse.

Claims 30 and 47 as amended are directed to methods of treating diffuse large B-cell lymphoma by oral administration once or twice daily for a total daily dose of 200-600 mg of pharmaceutical compositions comprising SAHA or pharmaceutical acceptable salt or hydrate thereof.

Richon is fatally deficient. Richon is based on the discovery that HDAC inhibitors induce expression of a thioredoxin-binding protein-2 which is further associated with a decrease in the level or activity of thioredoxin (TRX). However, although Richon refers to use of HDAC inhibitors in a laundry list of TRX-mediated diseases (see [0017] US 2003/0235588), Richon does not mention treatment of lymphoma and certainly not diffuse large B-cell lymphoma.

Further, Richon does not teach or suggest the claimed dosages and dosing schedules for treating diffuse large B-cell lymphoma. Specifically, Richon does not teach or suggest an instant method comprising orally administering to the subject once or twice daily for a total daily dose of 200-600 mg of SAHA, as required by independent claims 30 and 47 and the claims that depend therefrom. Nor does Richon teach or suggest the specific 400 mg once daily and 300 mg twice daily three days a week schedules recited in claims 70 and 71, respectively.

Rubartelli does not remedy the deficiencies of Richon. First, Rubartelli concludes that different cell types respond differently to thioredoxin. Second, there is no teaching or suggestion in Rubartelli of the claimed doses and dosing schedules for oral treatment of patients with diffuse large B-cell lymphoma. To the contrary, Rubartelli is silent regarding to oral administration of SAHA once or twice daily for a total daily dose of 200-600 mg as recited in independent claims 30 and 47 and the claims that depend therefrom. Nor does Rubartelli teach or suggest the specific 400 mg once daily and 300 mg twice daily three days a week schedules recited in claims 70 and 71, respectively. In fact, the Examiner concedes that Richon and Rubartelli do not disclose instantly claimed specific administration schedules.

For these reasons, Richon and Rubartelli fail, alone or in combination, to teach or suggest the claimed invention. At best, the rejection amounts to an 'obvious to try" standard to determine the dosages of SAHA claimed here for treatment of diffuse large B-cell lymphoma. However, "obvious to try" is not the relevant standard for obviousness and the Section 103 rejection must fail for this reason as well.

Claims 41-45, 57-61, 67-68 and 71 are being rejected under 35 USC § 103(a) as being allegedly obvious over Richon and Rubartelli as applied to claims 30, 32-35, 37-40, 46-47, 49-56, 62-66 and 69-70 above and further in view of Kelly et al (Proc. American Society of Clinical Oncology, 2001, 20:87a, Abstract No.344, "Kelly"). As noted above, the Examiner concedes that Richon and Rubartelli do not disclose instantly claimed doses and specific administration schedules.

As discussed above, Richon and Rubartelli are fatally deficient. Combining Richon and Rubartelli with Kelly, does not cure the fatal deficiencies of the combination. There is no teaching in Kelly as to oral dosages SAHA at all -- and certainly no mention of the oral doses or schedules in independent claims 30, 47, 70 and 71 of SAHA for treatment of diffuse large B-cell

lymphoma. The objective of Kelly is to define a safe intravenous dosing schedule for SAHA in patients. As the evidence made of record with Applicants' September19, 2006 Amendment demonstrates, oral dosing of SAHA produces an unexpected increase in half life compared to IV delivery of SAHA. For this reason, Kelly cannot cure the deficiencies of Richon and Rubartelli. The rejection should be withdrawn.

Claims 30, 32-35, 37-47 and 49-71 are rejected under 35 U.S.C. § 103(a) as being allegedly obvious over Breslow et al (U.S Patent No. 5,700,811, "Breslow") in view of Richon. Applicants traverse.

Breslow is fatally deficient. Breslow does not teach or suggest treatment of diffuse large B-cell lymphoma at all. Nor does Breslow teach or suggest the claimed dosages and dosing schedules for treating diffuse large B-cell lymphoma. Specifically, Breslow does not teach or suggest an instant method comprising administering to the subject once or twice daily for a total daily dose of 200-600 mg of SAHA as stipulated in independent claims 30 and 47 and the claims that depend therefrom. Nor does Breslow teach or suggest the specific 400 mg once daily and 300 mg twice daily three days a week schedules recited in claims 70 and 71, respectively. Combination with Richon does not overcome this deficiency. As discussed above, Richon is fatally deficient, since (a) Richon does not mention treatment of lymphoma and certainly not diffuse large B-cell lymphoma and (b) Richon does not teach or suggest the claimed dosages and dosing schedules for treating diffuse large B-cell lymphoma. Combining Breslow and Richon does not cure the fatal deficiencies of the combination. The rejection should be withdrawn.

CONCLUSION

Favorable action on the merits is respectfully requested. If any discussion regarding this Response is desired, the Examiner is respectfully urged to contact the undersigned at the number given below, and is assured of full cooperation in progressing the application to allowance.

Respectfully submitted,

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